

# IMPLANTABLE MATERIAL FOR THE REPAIR, AUGMENTATION, OR REPLACEMENT OF BONE AND A METHOD FOR THE PREPARATION THEREOF

## TECHNICAL FIELD

[0001] The present invention relates generally to an implantable material and a method for the preparation thereof. The material is useful, for example, for the repair, augmentation, or replacement of substantially all or part of one or more bones, or as a substitute for bone grafts in orthopaedic applications.

## BACKGROUND OF THE INVENTION

[0002] Except where specified below the term 'fibroin' is used to refer generically to the main structural protein of cocoon silks whether they are derived from the domesticated Mulberry Silkworm (*Bombyx mori*), a transgenic silkworm or from any Wild Silkworm including, but not limited to those producing Muga, Eri or Tussah silks.

[0003] Furthermore, the term 'silk' is used to refer to the natural fine fibre that silkworms secrete, which mainly comprises the two proteins, fibroin and sericin, fibroin being the principal structural material in the silk, and sericin being the material surrounding the fibroin and sticking the fibres together in the cocoon.

[0004] 'Silk cocoon' is used to refer to the casing of silk spun by the larvae of the silk worm for protection during the pupal stage.

[0005] The term 'bone repair' refers to any procedure for repairing bone, including those which use a material as a substitute for bone grafts.

[0006] The term 'bone augmentation' refers to the use of any procedure for adding or building bone.

[0007] The term 'bone replacement' refers to the use of any procedure for replacing existing bone.

[0008] The term 'polymer' is used to refer to all large molecules comprised of chains of one or more types of monomeric units and includes macromolecular proteins.

[0009] There are a number of injuries and conditions that require surgical intervention to repair, augment, or replace substantially all or part of one or more bones. These conditions include, for example, traumatic fractures, non-unions, bone cysts, critical bone defects, loosening of prostheses at the bone/prosthesis interface and malignant tumours in bone.

[0010] Historically, many of these conditions could only be repaired by autografts (where tissue is transplanted from one part of the body to another in the same individual, also called an autotransplant), or allografts (where an organ or tissue is transplanted from one individual to another of the same species with a different genotype, also called an allogeneic graft or a homograft) using materials derived from bone.

[0011] Autografts are currently the favoured option for bone repair. However autografting has several associated problems, including the high costs for the surgical harvesting procedure and pain and morbidity experienced at the harvest site. For example, harvesting a graft from the iliac crest, the protruding bony section of the patient's hip, can cost between \$1,000 to \$9,000 per procedure for the harvesting operation and the additional hospital stay. Where morbidity is experienced at the harvest site, symptoms include pain, infection, nerve damage and blood loss, the latter often requiring blood transfusion associated with the risk of blood borne infection.

The quantity of bone tissue that can be harvested is limited and can be of poor quality especially in osteoporotic patients.

[0012] Allograft materials taken from cadavers circumvent some of the shortcomings of autografts by eliminating donor site morbidity and issues of limited supply as taught by Burkuss, J. K. (2002) in his article "New Bone Graft Techniques and Applications in the Spine" in Medscape today (<http://www.medscape.com/viewarticle/443902>). However, the use of allografts presents additional risks and problems not seen with autografts. In an allograft, because the tissue is obtained from a donor, there is a risk of disease transmission from donor to recipient and it has been established that HIV/hepatitis can be transmitted through allografts. In addition, allografts and allogenic implants are acellular and are less successful and less predictable than autografts for reasons attributed to immunogenicity and the absence of viable cells that become osteoblasts.

[0013] Due to the shortcomings of autografts and allografts, efforts have been made to find suitable bone repair materials (BRMs) for use as alternatives to autografts and allografts. However, BRMs have not yet replaced autografts, because in the past they have failed to adequately address five main criteria: load bearing ability; osteoconductivity; osteoinductivity; resorbability (as taught by Rose, F. R. A. J., and Oreffo, R. O. C. (2002) in their article "Bone Tissue Engineering: Hope vs Hype." Published in Biochem. Biophys. Res. Commun 292, 1-7); and ease of use in theatre. Ease of use in theatre is of considerable importance and is not met by many artificial BRMs.

[0014] Ideally, BRMs need to be able to be capable of full and immediate load-bearing. In this context, load-bearing can be defined as the ability of a BRM to maintain its mechanical integrity without undue distortion when subjected to the forces applied to it in the course of normal everyday life without recourse to secondary supporting structures, such as pins, plates, external fixators, and casts. Furthermore, immediate load bearing can be defined as the ability of the repair to bear full loads by the time the patient has recovered from anaesthesia.

[0015] The material properties that enable immediate load bearing of the BRM depends on the location into which the BRM is to be implanted, but includes good compressive toughness, good compressive strength, good compressive elastic modulus and good interfacial properties with the existing bone. It is clear that the minimum requirement for immediate load bearing is for the strength and toughness of the material to match that of healthy bone at the site of implantation. Furthermore, it is generally understood that BRMs need to mimic the properties of bone fairly closely to prevent high local stress concentrations or stress shielding, both of which are likely to adversely affect natural bone adjacent to the implanted BRM. Thus it is highly desirable to use the mechanical properties of normal bone as target values for load bearing BRMs.

[0016] Toughness provides resistance to fracture and is extremely important in bone. Toughness is measured in units of joules per cubic metre ( $\text{Jm}^{-3}$ ). There are several methods for measuring the toughness of bones and the values obtained depend to an extent on the method that is used and the exact conditions of specimen loading. However, for a mid-diaphyseal femur of a healthy 35 year old, the work of fracture method, the impact of notched bone method and the J-integral method all gave similar results of  $3.9 \text{ kJ m}^{-3}$ ,  $2.0 \text{ kJ m}^{-3}$  and  $1.3 \text{ kJ m}^{-3}$ , respectively (disclosed by Zioupos, J. in his